CLAIMS

1. A method for the enantioselective preparation of sulfoxides derivatives or basic salts thereof,
characterized in that an enantioselective oxidation of a sulphide of the following general formula (I)

$$A - CH_2 - S - B \qquad (I)$$

wherein A is a diversely substituted pyridyl nucleus and B a heterocyclic residue comprising a benzimidazole or a imidazo-pyridyl nucleus,
is performed using an oxidizing agent in the presence of a tungsten- or vanadium-based catalyst and of a chiral ligand, followed if necessary by a salification by a base, in order to obtain the sulfoxide $A - CH_2 - SO - B$ (Ia).

2. A method according to claim 1, characterized in that, in general formula (I), a pyridyl group or a pyridyl group bearing one or more substituents selected from the linear or branched alkyl groups of 1 to 6 carbon atoms, linear or branched alkoxy groups of 1 to 6 carbon atoms, methyl or ethyl groups substituted by one or several halogen atoms, amino, alkylamino or dialkylamino groups where the alkyl moiety, whether linear or branched, comprises 1 to 5 carbon atoms ; B represents a heterocycle selected from the benzimidazole or imidazo-[4,5-b]-pyridyl groups, substituted if necessary by one or several linear or branched alkyl groups of 1 to 6 carbon atoms, linear or branched alkoxy groups of 1 to 6 carbon atoms.

3. A method according to claim 2, characterized in that the A and B groups are substituted on one or several carbon atoms by a methyl, ethyl, methoxy or trihalogenomethyl group.

4. A method according to claim 3, characterized in that A is a 2-pyridyl group substituted by one or several methyl, ethyl, methoxy or trifluoromethyl groups.

5. A method according to any of claims 3 and 4, characterized in that A is a 4-methoxy-3,5-dimethyl-2-pyridyl

group and B is a 5-methoxy-1H-benzimidazolyl or 5-methoxy-imidazo-[4,5-b]-pyridyl group.

6. A method acccording to any of the preceding claims, characterized in that the obtained enantiomer is salified by reaction with basic mineral reagents comprising alcaline or earth-alcaline counter ions.

7. A method according to claim 6, wherein the salt is a sodium, potassium, lithium, magnesium or calcium salt.

8. A method according to any of claims 1 to 7, wherein the oxidant is a peroxide or a hydroperoxide.

9. A method according to claim 8, wherein the oxidant is hydrogen peroxide, urea-H_2O_2 (UHP) or cumene or tertiobutyl hydroperoxide.

10. A method according to any of claims 1 to 9, wherein the catalyst is a (V) oxo-vanadium complex or a derivative of tungsten.

11. A method according to claim 10, wherein the complex or the derivative is prepared from tungsten trioxide, vanadium acetylacetonate, or vanadium sulphate.

12. A method according to any of claims 1 to 11, characterized in that the catalyst is vanadium based and the ligand is tridentate.

13. A method according to any of claims 1 to 12, characterized in that the ligand is represented by the following general formula (II) :

$$RO\text{-}CR_1R_2\text{-}CR_3R_4\text{-}NR_5R_6$$

where **R** is a hydrogen atom or a linear or branched alkyl group of 1 to 6 carbon atoms or an aryl or heteroaryl group ;

$\mathbf{R_1}$ to $\mathbf{R_4}$, which can be the same or different, represent a linear or branched alkyl group of 1 to 6 carbon atoms, possibly comprising a heteroatom such as sulphur, nitrogen and oxygen and/or substituted by an amino group ; an aryl group ; an alkylaryl group ; an alkoxycarbonyl group ; a heteroaryl group or a heterocyle ; a heteroarylalkyl or a heterocyclalkyl group, with the proviso that R_1 should not be identical with

R_2, and/or R_3 should not be identical with R_4, so that the ligand comprises one, or two asymmetry centers ;

R_1 and **R_2** together can represent a carbonyl group C=O ;

R_1 and **R_3**, or **R_2** and **R_4** together, can form a carbon ring having 5 or 6 carbon atoms or a bicyclic system with 9 or 10 carbon atoms where one of the cycles can be aromatic ;

R_4 and **R_5**, which can be the same or different, can form a 5- or 6-membered heterocycle with the nitrogen atom ;

R_5 and **R_6**, which can be the same or different, represent a linear or branched alkyl group of 1 to 6 carbon atoms or a 5 or 6-membered carbon ring, or form a heterocycle with the nitrogen atom to which they are bound, or

R_5 and **R_6** represent, together with the nitrogen, a -N=CHAr double bond where **Ar** is a aryl residue, possibly substituted by 1 to 3 groups, and preferably bearing a hydroxyl group.

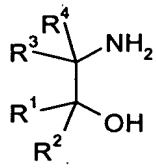
14. A method according to claim 13, characterized in that **Ar** is a 2'-hydroxyphenyl group possibly substituted on the aryl group.

15. A method according to claims 13 or 14, characterized in that **R_1** and **R_3**, or **R_2** and **R_4**, represent an hydrogen atom, whereas **R_2** and **R_4**, or **R_1** and **R_3**, respectively, are linear or branched alkyl groups of 1 to 6 carbon atoms, a aryl group or form together a carbon ring having 5 or 6 carbon atoms or a bicyclic system with 9 or 10 carbon atoms where one of the cycles can be aromatic.

16. A method according to any of claims 13 to 15, characterized in that the aryl group is selected from the phenyl group, the naphtyl group, the tetrahydronaphtyl group, the indanyl group and the binaphtyl group, where the aryl group can be substituted by 1 to 3 substituents selected from a hydroxyl group, a linear or branched alkyl group comprising 1 to 4 carbon atoms, a nitro group, a (C_1-C_4)alkoxy group and a halogen atom.

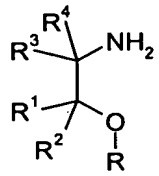
17. A method according to any of claims 13 to 16, characterized in that the ligand of formula (II) is alternatively derived from:

- an amino-alcool of formula (III)


(III)

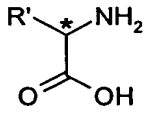
wherein $\mathbf{R_1}$, $\mathbf{R_2}$, $\mathbf{R_3}$ and $\mathbf{R_4}$ are as defined in any of claims 13 to 16,

- an amino-ether of formula (IV)


(IV)

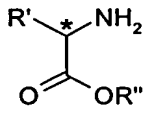
wherein **R**, $\mathbf{R_1}$, $\mathbf{R_2}$, $\mathbf{R_3}$ and $\mathbf{R_4}$ are as defined in any of claims 13 to 16,

- an amino acid of formula (V)


(V)

wherein **R'** takes the definition of R_3 or R_4 according to any of claims 13 to 16 or,

- an amino-ester of formula (VI)

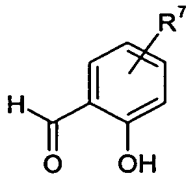

(VI)

wherein **R'** takes the definition of R_3 or R_4 according to anyone of claims 13 to 16 and **R''** takes the definition of R according to any of claims 13 to 16.

18. A method according to claim 17, characterised in that the amino-alcohol of formulae (III) is selected from L- or D-valinol, *R-tert*-leucinol, *S-tert*-leucinol and (1*S*,2*R*)-(-)- or (1*R*,2*S*)-(+)-1-amino-2-indanol and in that the amino acid of formulae (V) is selected from L-valine or D-valine, L-phenylalanine or D-phenylalanine, L-methionine or D-methionine, L-histidine or D-histidine, L-lysine or D-lysine.

19. A method according to any of claims 13 to 18, characterized in that the ligand of formula (II) is obtained

by reacting an amino-alcohol, an amino-ether, an amino acid or an amino-ester of formulae (III), (IV), (V) and (VI), respectively, as defined in claims 17 or 18 with an aldehyde of salicylic acid, of formula (VII)



(VII)

wherein R_7 represents 1 to 2 substituents chosen independently ones of the others among an hydroxyl group, a linear or branched alkyl group containing from 1 to 4 carbon atoms, a nitro group, a (C_1-C_4)alkoxy group and a halogen atom.

20. A method according to any of claims 13 to 19, characterized in that a catalyst prepared from vanadium acetylacetonate and a ligand derived from an amino-alcool or an amino-ether respectively of formulae (III) or (IV) as defined in claim 17 or 18, are used.

21. A method according to claim 20, characterized in that the ligand of formula (II) is derived from an amino-alcohol of formula (III) as defined in claim 17, for which

R_5 and R_6 represent together with the nitrogen atom a double bind -N=CHAr, wherein **Ar** is an aryl group containing from 1 to 3 substituants and at least an hydroxyl group, **Ar** being preferably a phenyl group,

R_1 and R_3, or R_2 and R_4, represent an hydrogen atom, whereas R_2 and R_4, or R_1 and R_3, respectively, are, independently ones of the others, linear or branched alkyl groups of 1 to 6 carbon atoms, preferably a *tert*-butyl group or form together a carbon cycle of 5 or 6 carbon atoms or a bicyclic ring system of 9 or 10 carbon atoms wherein one of the cycles may be aromatic, preferably indanyl.

22. A method according to any of claims 13 to 19, characterized in that a catalyst prepared from vanadium sulphate and a ligand derived from an amino acid or an amino-

ester respectively of formulae (V) or (VI), as defined in claim 17 or 18, are used.

23. A method according to any of claims 1 to 21, characterized in that the ligand is 2,4-di-*tert*-butyl-6-[1-*R*-hydroxymethyl-2-methyl-propylimino)-methyl]-phenol, le 2,4-di-*tert*-butyl-6-[1-*S*-hydroxymethyl-2-methyl-propylimino)-methyl]-phenol, le (1*R*, 2*S*)-1-[2-hydroxy-3,5-di-*tert*-butyl-benzylidene)-amino]-indan-2-ol or (1*S*, 2*R*)-1-[2-hydroxy-3,5-di-*tert*-butyl-benzylidene)-amino]-indan-2-ol.

24. A method according to claim 23, characterized in that the ligand is in an acetonitrile solution.

25. A method according to claim 23 or 24, characterized in that an enantioselective oxidation of 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridyl)methyl]thio]imidazo[4,5-b]pyridine is carried out to obtain (-)-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridyl)methyl]sulfinyl]imidazo[4,5-b]pyridine by using a vanadium-based catalyst associated with a ligand consisting of 2,4-di-*tert*-butyl-6-[1-*R*-hydroxymethyl-2-methyl-propylimino)-methyl]-phenol or (1*R*, 2*S*)-1-[2-hydroxy-3,5-di-*tert*-butyl-benzylidene)-amino]-indan-2-ol in an acetonitrile solution, whilst the sulphide is in a methylene chloride or acetone or N-methylpyrrolidinone solution, respectively.

26. A method according to any of claims 10 or 11, characterized in that the catalyst is a tungsten derivative and the ligand is hydroquinine 2,5-diphenyl-4,6-pyridinyl diether $(DHQ)_2$-PYR or hydroquinidine 2,5-diphenyl-4,6-pyridinyl diether $(DHQD)_2$-PYR.

27. A method according to claim 26, characterized in that an eniantoselective oxidation of 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridyl)methyl]thio]imidazo[4,5-b]pyridine is carried out by hydrogen peroxide in the presence of tungsten trioxide and of $(DHQD)_2$-PYR in order to obtain the (-)-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridyl)methyl]-sulfinyl]imidazo[4,5-b]pyridine.

28. A method according to any of the preceding claims characterized in that the oxidation reaction is carried out in a solvent, in a neutral or weakly basic medium.

29. A method according to claim 28, characterized in that the solvent is a mixture of solvents consisting of a sulphide specific solvent and a ligand specific solvent selected from methanol, tetrahydrofuran, dichloromethane, acetonitrile, toluene, acetone, chloroform, dimethylformamide and N-methylpyrrolidinone, alone or in admixture, and the base is a tertiary amine selected from pyridine, di-isopropyl-ethylamine and triethylamine.